The reference Essenfeld et al. discloses a method for processing pathological *tissue* specimens more rapidly than conventional methods. The Essenfeld et al. fixative solution consists of "a fixative and dehydrating agent" - - an alcohol *and* a ketone. The method of the present invention does not require both components. Furthermore, Essenfeld et al. disclose the use of a surfactant at "about 1%" of total volume. Essenfeld et al. include DMSO in their list of surfactants. Essenfeld et al. do not provide any teaching that would indicate utilizing surfactant at 50% of total volume. Essenfeld et al. do not teach or suggest using their solution with specimens other than tissue.

Applicants respectfully submit that the Examiner's specific comments regarding Essenfeld et al are not consistent with what is actually stated in Essenfeld et al. The method taught in Essenfeld et al is not even remotely close to the method of the claimed invention, nor are the specific amounts of components.

Although the claims have been rejected as anticipated under 35 U.S.C. §102 on the disclosure of Essenfeld et al., it is axiomatic that anticipation under Section 102 requires that the prior art reference disclose every element of the claim. In re King, 801 F.2d 1324, 1326, 231 U.S.P.Q. 136, 138 (Fed. Cir. 1986). Thus there must be no differences between the subject matter of the claim and the disclosure of the prior art reference. Stated in another way, the reference must contain within its four corners adequate directions to practice the invention. The corollary of this rule is equally applicable. The absence from the reference of any claimed element negates anticipation. Kloster Speedsteel AB v. Crucible Inc., 793 F.2d 1565, 1571, 230 U.S.P.Q. 81, 84 (Fed. Cir. 1986)

Here is it clear that Claim 13 and all claims dependent thereon differ from Essenfeld et al. Clearly, Kloster Speedsteel shows that the cited art falls far short of the statutory standard of 35 U.S.C. 102. Claims 13-16, 18, 25, 26 and 31 are not anticipated by Essenfeld et al. Withdrawal of the instant rejection under Section 102 is therefore respectfully requested.

The Examiner has alleged that Claims 19, 20, 22 and 32 are rendered obvious under 35 U.S.C. §103 by Essenfeld et al. Claims 27-30 have been rejected under 35 USC Section 103 as allegedly rendered unpatentable by Essenfeld et al. in view of Evinger-Hodges et al. Claims 21, 23 and 24 have been rejected under 35 USC Section 103 as allegedly rendered unpatentable by Essenfeld et al in view of Rogers. Claims 13-16, 21, 25, 26, 28 and 31 have been rejected under 35 USC Section 103 as allegedly rendered unpatentable by Rogers. The cited prior art does not teach or suggest the claimed invention.

The present invention describes a method for stabilizing the nucleic acids of at least one cell in a sample, wherein said method comprises:

(a) adding to a vessel containing the sample, a composition comprising: (i) a first substance having a concentration effective for precipitating or denaturing proteins, comprising at least one alcohol or ketone whose concentration is less than 80% of the total composition; and a second facilitator substance not chemically related to the first substance having a concentration effective for aiding in the infusion of the first substance into said at least one cell whose concentration is greater than 20% of the total composition, wherein the combined concentrations of said first and second substances is equal to 100% of said composition;

(b) contacting said at least one cell in said sample with said composition;

(c) incubating said sample with said composition for an effective period of time and at an effective temperature; and

(d) obtaining said at least one cell with stabilized nucleic acids in said sample.

As stated above, Essenfeld et al. discloses a method for processing pathological tissue specimens more rapidly than conventional methods. Essenfeld et al. do not remotely teach or suggest the method of the present invention.

Evinger-Hodges et al. disclose an *in situ* procedure for detecting small numbers of nucleic acid molecules in cells or tissue specimens. Evinger-Hodges et al. test tissue samples for marker molecules, and describe a method for assaying biopolymers in specimens with intact membranes, which is entirely different from the method of the present invention. Applicants respectfully submit that Evinger-Hodges is not a properly cited reference. Furthermore, the Examiner has utilized Evinger-Hodges to make numerous inappropriate extrapolations with respect to time and temperature conditions (i.e., from 180 minutes to 3-4 days [72-96 hours is not the same as 3 hours and no one of ordinary skill in the art would make the leap to 72-96 hours improperly suggested by the Examiner] and the reference to room temperature).

Rogers discloses a method to clarify and contrast stain intact biological tissue samples for microscopic analysis. The Examiner has made numerous improper assumptions that Rogers teaches or renders obvious the claimed invention. This is simply incorrect. No concentrations are described in the Rogers reference; the claimed invention sets forth specific concentrations of components which are distinctly different from the Rogers reference. For example. in Rogers at Col. 4, Lines 54-56, methanol/DMSO/30% H2O2 is used, and the present invention does not have H2O2. In Rogers at Col. 4, Lines 60-63, the suggestion is made that one can do the staining first, presumably with a methanol/DMSO mixture, but Rogers does not provide a concentration for such a mixture. In Rogers at Col. 6, Lines 14-19, the method therein calls for 4 parts methanol, 1 part DMSO and 30% H2O2. Again, this is totally different from the present invention. Furthermore, the Examiner's comments about evaporation, spillage, etc. presume facts not proven or easily demonstrable.

Applicants respectfully submit that the method described in Rogers is therefore entirely different from the method of the claimed invention.

Thus Applicants respectfully submit that Rogers does not teach or suggest the claimed invention. The combination of Essenfeld et al. and Rogers does not teach or suggest the claimed invention. The combination of Essenfeld et al and

Evinger-Hodges et al. also does not teach or suggest the claimed invention. Each of the combinations, in fact, teach an entirely different method from the claimed invention.

It is well established that obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination, Carella v. Starlight Archery, 804 F.2d 1356, 231 U.S.P.Q. 644 (Fed. Cir. 1986). In determining obviousness, the inquiry is not whether each element existed in the prior art, but whether the prior art made obvious the invention as a whole for which patentability is claimed. Hartness International, Inc. v. Simplimatic Engineering Co., 189 F.2d 1100, 2 U.S.P.Q. 2d 1826 (Fed. Cir. 1987). Furthermore, the Examiner cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to depreciate the claimed invention, In re Fine, 837 F.2d 1071, 5 U.S.P.Q. 2d 1596 (Fed. Cir. 1988), which the Examiner has clearly done in order to reject the claims under 35 U.S.C. §103.

Applicants have carefully studied the cited art as applied by the Examiner to reject the present claims and respectfully assert that the cited art does not render the teachings of the present invention obvious to one of ordinary skill in the art. Therefore, it is believed that the rejections of the claims under 35 U.S.C. §103 is improper, and withdrawal of this rejection is respectfully requested.

In view of the above Remarks, it is believed that the present application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

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